UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/932,227	09/17/97	FOSSEL	E

EXAMINER

IM22/0425

LORUSSO & LOUD
440 COMMERCIAL STREET
BOSTON MA 02109

MULLIS, J

ART UNIT	PAPER NUMBER
1711	13

DATE MAILED: 04/25/00

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)
*U.S. GPO: 1996-404-496/40510

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/932,277	Fossel et al.
Examiner	**Group Art Unit**
Jeffrey Mullis	1711

☒ Responsive to communication(s) filed on *Feb 7, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *33-35, 38-44, 47-53, and 56-63* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *33-35, 38, 42-44, 50-53, and 59-63* is/are rejected.

☒ Claim(s) *39-41, 47-49, and 56-58* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

All remaining rejections and/or objections follow.

Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50 is unclear in that this claim depends from (preceding) cancelled claims such as claims 46, 45, 37 and 36.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 33-34, 38, 51-53 and 59 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weuffen et al. (USP 5,629,002).

See the Office action of Paper No. 6 at page 4 lines 5 et seq.

Claims 33-34 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hechtman (USP 5,595,753).

See the Office action of Paper No. 6 at the paragraph bridging pages 4 and 5 et seq.

Claims 33-35, 38, 42-44, 50-53 59 and 61-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garfield et al. in view of Hechtman, Altadonna (USP 5,853,768), Cooke et al. (USP 5,428,070), Saavedra et al. (USP 5,632,981) and Cooper et al.

See the Office action of Paper No. 8 at the paragraph bridging pages 3 and 4 et seq.

Claims 39-41, 47-49 and 56-58 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's arguments filed 2-7-00 have been fully considered but they are not deemed to be persuasive.

Applicant argues that there is no hostile biophysical environment in any example in the Weuffen reference because the ionic strength of the Weuffen composition is less than that of blood. However applicants have not submitted any proof the composition must have a higher ionic strength than that of blood

in order to create a hostile biophysical environment. Applicants argue that the reference contains sorbitol and xylitol which would draw molecules like L-arginine out of the tissue rather than aid in getting them across the skin into cells and fluid of the scalp. It is apparent however that at least some components of the Weuffen reference must migrate through the skin or else the arginine of the Weuffen process would have no purpose. It is not clear why some components would migrate and the arginine wouldn't. In any case, such characteristics are applicant's burden to prove as set out above.

With regard to Hechtman, applicant again argues that the reference discloses no compositions having a hostile biophysical environment. Applicant argues that "although L-arginine is used by Hechtman, it is not clear that it actually does anything". However the mere fact that it may not be clear that a particular composition has a particular characteristic is not pertinent as set out above. This is applicant's burden to prove. Although applicant says that there is no dose response for L-arginine, since all doses are equally effective within any kind of experimental error, a drug's effectiveness does not continue to increase without limit with the amount administered. Furthermore the sphincter pressure at 10 minutes is lowest for the 10 milligram dose, second lowest for the 1 milligram dose and third lowest for the 0.1 milligram dose despite the fact that the

sphincter muscle pressure is highest for the 10 milligram dose to begin with. The fact that this relationship may not hold at higher time levels possibly only indicates that optimal dosage was previously reached prior to these time periods. Furthermore, patentees disclose at column 4, lines 56-57 that no effect is noted at very low L-arginine concentrations. This indicates that L-arginine does have an effect on sphincter muscle pressure. Applicant continues to argue that it is not clear that L-arginine is doing anything in the Hechtman reference. However the claims of the patent specifically recite that arginine is administered in an amount effective to treat a condition in claim 1 of the patent. A U.S. patent has the presumption of validity and therefore it must be presumed that L-arginine is effective.

With regard to the rejections under 35 U.S.C. § 103, applicant argues that the only relevant references are those which disclose some feature of applicant's invention. With regard to Altadonna and Cooper, applicants argue that these references do not teach the creation of an hostile biophysical environment as claimed to drive L-arginine from a delivery vehicle to the skin where it is absorbed by the tissue. While it may be true that Altadonna and Cooper do not teach driving L-arginine from a delivery vehicle to the skin, it is the position of the Examiner that these two secondary references teach enhancing the absorption of a medicament into the skin by the use

of ionic surfactant/salts. Patented claims are given their broadest reasonable interpretation and it is the position of the Examiner that a reasonable interpretation of the teachings of these two secondary references of enhanced penetration is embraced by applicant's limitation of a hostile biophysical environment since there is nothing in the specification to indicate that by "hostile biophysical environment" applicants mean anything more than an environment which enhances penetration. It is the position of the Examiner therefore that the concept of a hostile biophysical environment is taught by Altadonna and Cooper. Applicant argues that "but for such an hostile biophysical environment, the effects described in applicant's specification would not be produced and the effects of applicant's invention are an unexpected and surprising result". The Examiner assumes that the unexpected results being referred to are those associated with enhanced penetration. However enhanced penetration is taught by the secondary references Altadonna and Cooper.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Jeffrey Mullis at telephone number (703) 308-2820.

J. Mullis:cdc

April 21, 2000

JEFFREY C. MULLIS
PRIMARY EXAMINER
GROUP ~~1200~~ 1711